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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/551,341	04/18/00	BRASS C	IN01023K

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EXAMINER	
ANDRES, J	
ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 07/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/551,341	BRASS ET AL.	
	Examiner	Art Unit	
	Janet L Andres	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of interferon alpha 2b and ribavirin in combination with vitamin E or derivatives in Paper No. 8 is acknowledged. The traversal is on the ground(s) that Applicants are investigating the use of a combination of vitamins E and C as a therapeutic agent. This is not found persuasive because Applicant has not distinctly and specifically pointed out the supposed errors in the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-46 are pending in this application and are examined in light of Applicant's species election of interferon alpha-2b and vitamin E and derivatives.

Priority

2. Applicant's priority claim based on provisional application 60/129,991, filed 19 April 1999, is acknowledged.

Specification

3. The use of the trademarks has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

4. The specification is objected to because there are sequences on p. 21 that do not have sequence identifier numbers.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Although it is clear from the dependent claims that claim 1 is intended to include interferon treatment, it is in fact drawn to treatment with ribavirin and an antioxidant. This claim is examined as it appears it was intended to read.

7. Claims 2-6 are rejected under 35 U.S.C. 112, second paragraph because, due to the omission in claim 1, they lack an antecedent basis.

8. Claims 1-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "to lower viral RNA" or "to lower HCV-RNA". While "substantially lower" is defined in the specification, "lower" is not and thus one of skill in the art would not be able to determine the metes and bounds of the claims. The claims are further indefinite in the recitation of "ameliorate". Applicant does not set forth the limitations of amelioration.

9. Claims 1-6 are rejected as indefinite in the recitation of "susceptible viral infection". The metes and bounds of the claims can not be determined because the definition on p. 4 does not provide characteristics of those infections excluded.

10. Claims 13, 15, 16, 26-29, 34, and 42-46 are indefinite in the recitation of 3 MIU TIW, PO, and QW. These terms must be spelled out in the claims before abbreviations are used.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-9, 13-21, 26-38, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing hemolysis by administering vitamin E during treatment of hepatitis C with interferon and ribavirin, does not reasonably provide enablement for treatment of all viral infections or for use of any and all antioxidants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Interferons and ribavirin are used in combination to treat hepatitis C virus. Applicant lists a number of possible susceptible infections on p. 4-5 of the specification. However, Applicant has presented no objective evidence that would indicate that this combination could successfully be used to treat these or any other viral infections. *In vitro* efficacy is not readily predictive of therapeutic results; Applicant states on p. 5 (line 9) that efficacy of ribavirin is dependent on the site of the infection. No other guidance is provided, either in the specification itself or by teachings from the prior art. Thus one of skill in art would not predict that the combination therapy could be used to treat all viral infections and the specification does not provide guidance or teachings that would allow one of skill to determine which infections could be treated. In addition, the claims encompass all antioxidants. There are no teachings in the specification to allow one of skill to predict which ones could be used to inhibit hemolysis and further which ones could be successfully used in the claimed method of treatment. Thus one of skill in the art would not predictably be able to use the invention as broadly claimed. Without the ability to predict what diseases could be successfully treated, and what antioxidants could be

successfully used in the claimed methods of treatment, it would require undue experimentation for the skilled artisan to use the invention commensurate with the scope of the claims.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 1-16, 17-35, and 37-46 rejected under 35 U.S.C. 103(a) as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, vol. 339, pages 1485-1492), Davis et al. (New England Journal of Medicine, 1998, vol. 339, pages 1493-1499), Poynard et al. (The Lancet, 1998, vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, vol. 42, pages 731-747). McHutchison et al., Davis et al., Poynard et al., and Reichard et al. each teach the use of interferon a-2b in combination with ribavirin to treat hepatitis C. Each further teaches treatment courses of 24-48 weeks, interferon doses of 3 MIU TIW and ribavirin doses of 600-1200

mg/day. These references, however, fail to teach antioxidants to treat ribavirin-induced hemolysis. Vitamin E as an inhibitor of hemolysis is taught by Abella et al. Abella et al. teaches Vitamin E as a "well-known antioxidant" (abstract) and teaches decreased hemolysis when Vitamin E is administered (p. 740). Abella et al. fails to teach Vitamin E as an inhibitor of ribavirin-indiced hemolysis and does not teach Vitamin E derivatives. However, it would have been *prima facie* obvious to one of ordinary skill in the art to use Vitamin E to inhibit ribavirin-induced hemolysis because McHutchison et al., Davis et al., Poynard et al., and Reichard et al. each teach that this effect of ribavirin necessitated the reduction of ribavirin doses in several patients. One of ordinary skill would thus have been motivated to inhibit this hemolysis in order to maintain the desired dosage levels taught by each of these reports because each teaches that combination therapy is advantageous and that ribavirin was reduced or discontinued when hemolysis occurred. One of skill would predict, based on the teachings of Abella et al., that Vitamin E would be effective in this process and thus could be used to allow maintenance of ribavirin doses. Further, it would have been *prima facie* obvious to one of ordinary skill in the art to use derivatives directed to the same purpose, since one of ordinary skill would predict that they would have effects similar to the parent compound.

14. Claims 17 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over McHutchison et al. (New England Journal of Medicine, 1998, vol. 339, pages 1485-1492), Davis et al. (New England Journal of Medicine, 1998, vol. 339, pages 1493-1499), Poynard et al. (The Lancet, 1998, vol. 352, pages 1436-1422) or Reichard et al. (The Lancet, 1998, vol. 351, pages 83-87) in view of Abella et al. (Brit. J. Clin. Pharmacol., 1996, vol. 42, pages 731-747) as applied to claims 1-16, 17-35, and 37-46 above, and further in view of U.S. patent 4917888

(Katre et al., 1990). McHutchison et al., Davis et al., Poynard et al., Reichard et al., and Abella et al. teach as set forth above but fail to teach pegylated interferons. Pegylated of proteins including interferons is taught by the '888 patent. It would have been *prima facie* obvious to one of ordinary skill in the art to use pegylated interferons in the regimes taught by McHutchison et al., Davis et al., Poynard et al., Reichard et al. because the '888 patent teaches that pegylation of interferons increases their physiological half life and their solubility at physiological pH (column 1, column 4).

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 305-3014 or (703) 308-4242.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to **[yvonne.eyler@uspto.gov]**.

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly

signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
July 12, 2001

YVONNE EYLER, PH.D
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